

## **IN THE SPECIFICATION**

- (1) Delete the paragraph on page 26 lines 12-15 and replace it with:

FIG. 3 depicts the epicenter mapping of human chromosome region 19p12 amplicon, which includes EDG4 locus. The number of DNA copies for each sample is plotted on the Y-axis, and the X-axis corresponds to nucleotide position based on Human Genome Project working draft sequence (~~http://~~[genome.ucsc.edu/goldenPath/aug2001Tracks.html](http://genome.ucsc.edu/goldenPath/aug2001Tracks.html)).

- (2) Delete the paragraph on page 26 lines 16-20 and replace it with:

[0083] FIG. 4 depicts the epicenter mapping of human chromosome region 19p13 amplicon, which includes EDG5 and EDG8 loci. EDG5 is located at about 100 kilo bases from EDG8 in chromosome 19p13.3. The number of DNA copies for each sample is plotted on the Y-axis, and the X-axis corresponds to nucleotide position based on Human Genome Project working draft sequence (~~http://~~[genome.ucsc.edu/goldenPath/aug2001Tracks.html](http://genome.ucsc.edu/goldenPath/aug2001Tracks.html)).

- (3) Delete the paragraph on page 75 lines 13-20 and replace it with:

A TaqMan-based assay also can be used to quantify SPHK1, EDG4, EDG5, or EDG8 polynucleotides. TaqMan based assays use a fluorogenic oligonucleotide probe that contains a 5' fluorescent dye and a 3' quenching agent. The probe hybridizes to a PCR product, but cannot itself be extended due to a blocking agent at the 3' end. When the PCR product is amplified in subsequent cycles, the 5' nuclease activity of the polymerase, for example, AmpliTaq, results in the cleavage of the TaqMan probe. This cleavage separates the 5' fluorescent dye and the 3' quenching agent, thereby resulting in an increase in fluorescence as a function of amplification (see, for example, ~~http://~~[www2.perkin-elmer.com](http://www2.perkin-elmer.com) ).

- (4) Delete the paragraph on page 117 lines 13-27 and replace it with:

To determine the DNA copy number for each of the genes, corresponding probes to each marker were designed using PrimerExpress 1.0 (Applied Biosystems) and synthesized by Operon Technologies. Subsequently, the target probe (representing the marker), a reference probe

(representing a normal non-amplified, single copy region in the genome), and tumor genomic DNA (10 ng) were subjected to analysis by the TaqMan 7700 Sequence Detector (Applied Biosystems) following the manufacturer's protocol. The epicenter mapping around EDG4 gene was performed using amplified tumor and tumor cell line samples. Referring to FIG. 3, the EDG4 gene is indicated by an arrow. The amplified tumor samples used include 86-528, LUTU12, 106-192-0058, 144A1, 7476B1, 7464B1, 7468B1, 7483B1, and 7454B1. The number of DNA copies for each sample was plotted against genomic distance according to UCSC genome browser (<http://genome.ucsc.edu>) in FIG. 3. The number of DNA copies for each sample is plotted on the Y-axis, and the X-axis corresponds to nucleotide position based on Human Genome Project working draft sequence (<http://genome.ucsc.edu/goldenPath/aug2001Tracks.html>). FIG. 3 shows epicenter mapping of 19p12 amplicon, which includes the EDG4 locus. A full-length EDG4 gene was present at the epicenter.

(5) Delete the paragraph on page 120 lines 6-20 and replace it with:

To determine the DNA copy number for each of the genes, corresponding probes to each marker were designed using PrimerExpress 1.0 (Applied Biosystems) and synthesized by Operon Technologies. Subsequently, the target probe (representing the marker), a reference probe (representing a normal non-amplified, single copy region in the genome), and tumor genomic DNA (10 ng) were subjected to analysis by the TaqMan 7700 Sequence Detector (Applied Biosystems) following the manufacturer's protocol. The epicenter mapping around EDG5 gene was performed using amplified tumor and tumor cell line samples. Referring to FIG. 4, the EDG5 gene is indicated by an arrow. The amplified tumor samples used include CHTN875, CHTN883, CHTN885, CHTN890, CHTN894, 88-682, 88-249, 97-145, 90-794, and 90-594. The number of DNA copies for each sample was plotted against genomic distance according to UCSC genome browser (<http://genome.ucsc.edu>) in FIG. 4. The number of DNA copies for each sample is plotted on the Y-axis, and the X-axis corresponds to nucleotide position based on Human Genome Project working draft sequence (<http://genome.ucsc.edu/goldenPath/aug2001Tracks.html>). FIG. 4 shows epicenter mapping of 19p13.3 amplicon, which includes the EDG5 locus. A full-length EDG5 gene was present at the epicenter.

(6) Delete the paragraph on page 124 lines 3-18 and replace it with:

0397] To determine the DNA copy number for each of the genes, corresponding probes to each marker were designed using PrimerExpress 1.0 (Applied Biosystems) and synthesized by Operon Technologies. Subsequently, the target probe (representing the marker), a reference probe (representing a normal non-amplified, single copy region in the genome), and tumor genomic DNA (10 ng) were subjected to analysis by the TaqMan 7700 Sequence Detector (Applied Biosystems) following the manufacturer's protocol. The epicenter mapping around EDG8 gene was performed using amplified tumor and tumor cell line samples. Referring to FIG. 4, the EDG8 gene is indicated by an arrow. The amplified tumor samples used include CHTN875, CHTN883, CHTN885, CHTN890, CHTN894, 88-682, 88-249, 97-145, 90-794, and 90-594. The number of DNA copies for each sample was plotted against genomic distance according to UCSC genome browser (<http://genome.ucsc.edu>) in FIG. 4. The number of DNA copies for each sample is plotted on the Y-axis, and the X-axis corresponds to nucleotide position based on Human Genome Project working draft sequence (<http://genome.ucsc.edu/goldenPath/aug2001Tracks.html>). FIG. 4 shows epicenter mapping of 19p13.3 amplicon, which includes the EDG8 locus. A full-length EDG8 gene was present at the epicenter. EDG5 is located about 100 kilo bases away from EDG8 in Chromosome 19p13.3.